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GUIDELINES

# Chapter 1-6. Anaerobic infections (general): care needed when dealing with patients who have underlying diseases or complications



Classical anaerobic infections are so-called exogenous infections such as gas gangrene caused by *Clostridium* (*Clostridium perfringens*, etc.), tetanus due to *C. tetani* and botulism due to *C. botulinum*. Anaerobes are a component of the indigenous flora of the human skin, digestive tract and urogenital system. The density of bacteria found in the large intestine is 1,000 times and that in the oral cavity 10 times higher for anaerobes than for aerobes. About 100 types of anaerobes are isolated from clinical samples. Of all anaerobes isolated in laboratories, a third belong to the *Bacteroides fragilis* group (*B. fragilis*, *B. thetaiotaomicron*, *B. distasonis*, etc.), another third to the anaerobic gram-positive cocci such as genus *Peptostreptococcus* and the remainder are *Prevotella*, *Fusobacterium*, *Clostridium* and non-spore-forming gram-positive rods. These bacteria can be isolated from all parts of the body and can be responsible for various endogenous infections such as brain abscess and diabetic foot gangrene. Bacteria of genus *Actinomyces* and *Propionibacterium* are relatively resistant to oxygen and can induce skin and oral infections. Bacteria of genus *Bacteroides* and *Clostridium* can also survive oxygen-rich environments and cause soft tissue infections of usually aseptic areas in the vicinity of the digestive tract or in areas below the waist. Bacteria of genus *Fusobacterium*, *Prevotella* and *Porphyromonas* are also isolated from patients with head/neck including mouth or gastrointestinal infections, but they are susceptible to oxygen and die within 10–30 min if exposed to air.

Regarding the care needed when dealing with anaerobic infections which have developed in patients with underlying diseases or complications, we can say that special care is needed not only for prevention of infections in general but also for prevention of anaerobic infections in patients who are more likely than usual to develop such infections (e.g., patients with diabetes mellitus, malignant tumors or malignant hematological diseases, those receiving steroid therapy, and immunosuppressed patients). Because a high density of anaerobes is found in the indigenous flora, infection with a mixture of anaerobes and aerobes (pathogens for endogenous infection) can be more severe in these compromised hosts. Conditions characterized by a close association between anaerobic infection and a compromised host status are skin/soft tissue infections (foot gangrene, etc.) in diabetic patients and bacteremia/sepsis in patients with malignant tumors or hematopoietic diseases. From patients with diabetic foot gangrene, not only genus *Staphylococcus* but also anaerobic gram-positive cocci such as *Finegoldia magna* are often isolated. Gram-negative rods of genus *Bacteroides* and *Prevotella* are also isolated. In patients with malignant gastrointestinal tumors, bacteria of genus *Clostridium* such as *C. septicum*, *C. perfringens*, *C. clostridioforme* and *C. symbiosum* are sometimes isolated independently or in combination with a low density of some other bacteria from blood culture. In patients with hematopoietic diseases (neutropenia, myelogenous leukemia, etc.), blood culture sometimes reveals *Leptotorichia buccalis* or *Sneathia sanguinegens* which are simply indigenous bacteria in healthy individuals. In addition, bacteria of genus *Fusobacterium* may be isolated.

Many anaerobic infections generally involve multiple pathogenic bacteria. Surgical drainage, necrotic tissue removal and selection of antibiotics effective against both aerobes and anaerobes are essential for treatment. Because anaerobes grow slowly and take considerable time for culture, the time required until sensitivity test results are obtained is long, often forcing physicians to begin empirical treatment before such results become available. Antibacterial agents often selected for the treatment of

anaerobic infections are broad-spectrum agents. These include sulbactam/ampicillin, cefoxitin, imipenem/cilastatin and tazobactam/piperacillin. Chloramphenicol is effective against many anaerobes even at present, but it is seldom used nowadays because of serious adverse effects. Clindamycin is also used to deal with anaerobic infections, but, because of the resistance of some strains of the *B. fragilis* group, this drug has been increasingly replaced with other antibacterial agents, resulting in a decrease in the amount of this drug used. Metronidazole is not indicated for anaerobic infections in Japan, but this drug has excellent activity against anaerobes in general. When metronidazole is applied in an off-label fashion, care is needed because this drug exerts an antabuse-like action and adverse reactions such as central nervous system disorders can be induced by prolonged use or high-dose administration for non-indicated cases (i.e., use involving non-authorized methods or dose levels). In patients with uncompensated liver disease, the half-life of this drug is longer than usual, thus necessitating adjustment of the dose level. When other drugs are used as well, care is usually needed when administering the medication, with the features of individual patients (underlying diseases and complications) being taken into account.